EXPERT SYSTEM LICENSE EVALUATION
REPORT FOR LICENSE 04-00487-04 04-487-4 Revised as 4-487-7

NAME OF LICENSEE: US NAVAL RADIOLOGICAL DEFENSE LABORATORY
LISTED SITE: HISTOLOGICAL & MEDICAL SCIENCES DIVISION, SAN FRANCISCO 24, CA
TYPE OF ACTIVITY OR FACILITY: MEDICAL LICENSE - NUCLEAR MEDICINE PROGR

Description of LICENSEE ACTIVITY UNDER THIS LICENSE

USE OF K-42, BR-82, AND H-3 TO DETERMINE TOTAL BODY WATER AND EXCHANGE RATES IN HUMANS.

****
THERE WAS DEFINITE OR POSSIBLE HUMAN USE FOR THIS LICENSE
INDICATION OF POSSIBLE OR DEFINITE NONROUTINE USE IN HUMANS
****

---------- MATERIALS INFORMATION FOR THIS LICENSE ----------

--Information on type and form of materials--

--Authorized Material--	--Form Authorized--
H-3	Loose or Any
BR-82	Loose or Any
K-42	Loose or Any

AMOUNT OR ACTIVITY OF THOSE MATERIALS CONTRIBUTING TO INITIAL SCORE:

---Material--	-SLD/LOOSE--	-ACTIVITY-	
H-3	LOOSE	.05000000	CI

SCORE FOR H-3 is either 0 or not available

BR-82	LOOSE	.00900000	CI

SCORE FOR BR-82 is either 0 or not available

K-42	LOOSE	.00300000	CI

SCORE FOR K-42 is either 0 or not available

FINAL DECISION FOR LOOSE MATERIALS:

POTENTIAL SITE CONTAMINATION:
ELIMINATED FROM CONSIDERATION FOR SITE CONTAMINATION
Reason for elimination: LOW SCORE OF MATERIALS

SEQUENCE OF RECORDED REASONING

1. There was at least one sealed source on this license for which the amount remaining was reduced according to the length of the half-life

2. There was at least one loose material on this license for which the amount remaining was reduced according to the length of the half-life

3. FIRST SITE: The loose materials on this license were only short-lived materials, noble gases, or other materials which are not presently likely to produce significant contamination.

COMMENTS FOR LICENSE EVALUATION

Description of LICENSEE ACTIVITY UNDER THIS LICENSE

USE OF K-42, BR-82, AND H-3 TO DETERMINE TOTAL BODY WATER AND EXCHANGE RATES IN HUMANS.

- GENERAL COMMENTS ENTERED BY THE REVIEWER CONCERNING THE EVALUATION -
-- THE LICENSEE WAS AUTHORIZED 50 MILLICURIES OF TRITIUM IN THE FORM OF
-- WATER, 3 MILLICURIES OF BROMINE 82 IN THE FORM OF AMMONIUM BROMIDE,
-- AND 3 MILLICURIES OF POTASSIUM 42 IN THE FORM OF POTASSIUM CHLORIDE
-- FOR USE IN THE DETERMINATION OF TOTAL BODY WATER AND EXCHANGE RATES
-- IN 40 NORMAL ADULTS. BOTH MALE AND FEMALE VOLUNTEERS WERE TESTED.

END OF COMMENTS FOR LICENSE EVALUATION

--- EXPERT SYSTEM EVALUATION WAS BASED ON THE ---
---- FOLLOWING INVENTORY RECORD -----
REGION RESPONSIBLE: V
LICENSEE NAME: US NAVAL RADIOLOGICAL DEFENSE LABORATORY
STREET ADDRESS: HISTOLOGICAL & MEDICAL SCIENCE City: SAN FRANCISCO

FIPS state code (principal operation): CA
Site used: HISTOLOGICAL & MEDICAL SCIENCES DIVISION, SAN FRANCISCO 24, CA
Disposition information present: NO DISPOSITION INFORMATION GIVEN
This license was listed as expired on 05/31/59

APPLICATION INFORMATION

There WAS a licensee application contained in the file
The application contained some information on material use.
GENERAL INVENTORY RECORD COMMENTS.
H-3, K-42, AND BR-82 USED TO DETERMINE EXCHANGE RATES IN HUMANS.
JOB NUMBER: 1722 BOX NUMBER: 02

Date of last evaluation or revision: 06/30/94

FORM AEC-374
(12-57)

U. S. ATOMIC ENERGY COMMISSION
BYPRODUCT MATERIAL LICENSE

Pursuant to the Atomic Energy Act of 1954 and Title 10, Code of Federal Regulations, Chapter 1, Part 30, Licensing of Byproduct Material, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, own, possess, transfer and import byproduct material listed below; and to use such byproduct material for the purpose(s) and at the place(s) designated below. This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, and is subject to all applicable rules, regulations, and orders of the Atomic Energy Commission now or hereafter in effect and to any conditions specified below.

Licensee

1. **Name** U. S. Naval Radiological Defense Laboratory
2. **Address** Biological & Medical Sciences Division
San Francisco 24, California

3. License number 4-1874 (059)
4. Expiration date May 31, 1959
5. Reference No.

6. Byproduct material (element and mass number)	7. Chemical and/or physical form	8. Maximum amount of radioactivity which licensee may posses at any one time
A. Hydrogen-3	A. Tritiated water	A. 50 millicuries
B. Potassium-42	B. Chloride	B. 3 millicuries
C. Bromine-82	C. Ammonium bromide	C. 9 millicuries

9. Authorized use

A through C: Measure total exchangeable potassium, total exchangeable chloride and total body water simultaneously in a total of 40 normal adults.

CONDITIONS

10. Unless otherwise specified, the authorized place of use is the licensee's address stated in Item 2 above.
11. The licensee shall comply with the provisions of Title 10, Part 20, Code of Federal Regulations, Chapter 1, "Standards for Protection Against Radiation".
12. Byproduct materials shall be used by, or under the supervision of Elden A. Boling, M.D.
13. Byproduct material acquired from an Atomic Energy Commission facility shall not be used in humans until its pharmaceutical quality and assay have been independently established.
14. Total amount of Hydrogen 3 acquired under this license shall not exceed 50 millicuries.

For the U. S. Atomic Energy Commission

Date May 7, 1958

by (b) (6) Chief, Isotopes Branch
Division of Licensing and Regulation
Washington 25, D. C.

(b) (6)

1-12-57

Form AEC-313 (2-57)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved. Budget Bureau No. 38-R027.3.

INSTRUCTIONS.—Complete Items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail two copies to: U. S. Atomic Energy Commission, P. O. Box E, Oak Ridge, Tenn. Attention: Isotopes Extension, Division of Civilian Application. Upon approval of this application, the applicant will receive an AEC Byproduct Material License. An AEC Byproduct Material License is issued in accordance with the general requirements contained in Title 10, Code of Federal Regulations, Part 30 and the licensee is subject to Title 10, Code of Federal Regulations, Part 20.

1. (a) NAME AND STREET ADDRESS OF APPLICANT. *(Institution, firm, hospital, person, etc.)*

(b) (6) [redacted]
Chairman, Radioisotope Committee
U.S. Naval Radiological Defense Laboratory
San Francisco 24, California

(b) STREET ADDRESS(ES) AT WHICH BYPRODUCT MATERIAL WILL BE USED. *(If different from 1 (a).)*

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

[redacted] Scientific Department
Biological & Medical Sciences Division
Biochemistry Branch

3. PREVIOUS LICENSE NUMBER(S). *(If this is an application for renewal of a license, please indicate and give number.)*

License No. 4-487-3 (Expires 1/31/59)

4. INDIVIDUAL USER(S). *(Name and title of individual(s) who will use or directly supervise use of byproduct material. Give training and experience in Items 8 and 9.)*

(b) (6) [redacted] MD
LT (MC) USNR

5. RADIATION PROTECTION OFFICER *(Name of person designated as radiation protection officer if other than individual user. Attach resume of his training and experience as in Items 8 and 9.)*

(b) (6) [redacted]
Chairman, Radioisotope Committee
(Ref: Ltr 3-730-267 ALS:ams of 4 Dec 1956 w/att form AEC-313 and supplements).

6. (a) BYPRODUCT MATERIAL. *(Elements and mass number of each.)*	(b) CHEMICAL AND/OR PHYSICAL FORM AND MAXIMUM NUMBER OF MILLICURIES OF EACH CHEMICAL AND/OR PHYSICAL FORM THAT YOU WILL POSSESS AT ANY ONE TIME. *(If sealed source(s), also state name of manufacturer, model number, number of sources and maximum activity per source.)*	
Hydrogen 3	Hydrogen 3 - Tritiated Water (HTO)	50 millicuries
Potassium 42	Potassium chloride solution	3 millicuries
Bromine 82.	Ammonium bromide solution	9 millicuries

DUPLICATED
FOR DIV. OF INSP.

7. DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED. *(If byproduct material is for "human use," supplement A (Form AEC-313a) must be completed in lieu of this item. If byproduct material is in the form of a sealed source, include the make and model number of the storage container and/or device in which the source will be stored and/or used.)*

Supplement 1 (AEC-313A) is attached.

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(Continued on reverse side)

Form AEC 313a (3/56)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE—PAGE 1

Form approved. Budget Bureau No. 38-R027.3.

If byproduct material is for "human use" (internal administration of byproduct material or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

1.(a) Using physician's name

(b) (6) MD
LT (MC) USNR
U.S. Naval Radiological Defense Lab.
San Francisco 24, California

(b) Name & address of applicant (if different from 1(a))

(b) (6)
Chairman, Radioisotope Committee
U.S. Naval Radiological Defense Laboratory
San Francisco 24, California

2. The using physician indicated above is licensed to dispense drugs in the practice of medicine by a state or territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.	CIRCLE ANSWER	(Yes) No
3. A Supplement A—Human Use—Page 3 (statement of using physician's clinical radioisotope experience) is submitted in support of this application. If answer is NO, use reverse side of this page to explain or refer to other application or related documents on which this information appears.	CIRCLE ANSWER	(Yes) No

PROPOSED DIAGNOSIS OR TREATMENT

4. (a) Describe purpose for which byproduct material will be used including specific conditions or diseases to be diagnosed or treated: (Use reverse side if necessary).

Measurement of total exchangeable Potassium, total exchangeable chloride, and total body water simultaneously in healthy adult men and women.

(b) Chemical form administered: 1) Potassium chloride
2) Ammonium bromide
3) Enriched tritiated water

(c) Describe procedures which will be observed to minimize hazard from handling, storage, and disposal of the byproduct material:

1) Handling will be done by trained personnel using NRDL equipment.
2) Storage will be in 2 inch lead shielding.
3) K^{42} and Br^{82} will decay away. H^3 wastes will consist only of counting solutions.

(d) Description and sketches of special devices to be used for administering byproduct material to human beings are (1) Attached (Literature references will suffice).	CIRCLE ANSWER	(Yes) No
(2) On file with the Isotopes Extension. Refer to Application No: _____. See remarks(over)	CIRCLE ANSWER	Yes No

PROPOSED DOSAGE SCHEDULE

5. (a) In millicuries for internally administered byproduct material other than discrete fixed source; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.;) state separately for each condition or disease (use reverse side if necessary).

Potassium 42: 0.050 millicuries
Bromine 82: 0.010 millicuries
Hydrogen 3: 1.0 millicuries

} To be given as one single dose. (See 5b).

For total dose (rad) see 5(b) supplement.

(b) Investigative proposal for experimental, new or unusual human uses is attached. (Attachment should include outline of conditions to be evaluated, including data from animal studies and/or abstract of literature reference, if any, and number and type of patients (i.e., age group, moribund, etc.).) See Suppl. CIRCLE ANSWER (Yes) No

6. If byproduct material will not be obtained in precalibrated form for oral administration or in precalibrated and sterilized form for parenteral administration, describe identification, processing, and standardization procedures:

These will be carried out as follows: See reverse of page

7. The proposed use of byproduct material has been, or will be, approved by the medical isotope committee.	CIRCLE ANSWER	(Yes) No

HOSPITAL FACILITIES FOR INDIVIDUAL PRACTICE USE ONLY

8. (a) The applicant has completed arrangements for a hospital to admit radioactive patients whenever advisable.	CIRCLE ANSWER	Yes No
(b) A copy of instructions to be furnished to the hospital as to radiological safety precautions to be taken and available radiation instrumentation is attached.	CIRCLE ANSWER	Yes No

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Item 4(d): Doses will be administered to the human subjects by means of gravimetrically calibrated glass syringes in volumes of 20 ml, using isotonic sodium chloride solution as diluent.

(See Supplement 1 for Item 5(b).

Item 6:

H^3 will be obtained as sterile tritiated water.

K^{42} will be obtained as K^{42} in HCl. This will be processed as follows:

1) Shipment will be diluted to total volume of 20 ml/mc, using sterile isotonic saline as the diluent.
2) 1 N $NaHCO_3$ will be added using phenel red as indicator to the point of color change.
3) 1.0 ml of this material will be given to two 3 week mice, intraperitoneally, and they will be observed for one hour prior to use of the material.
4) The diluted and neutralized shipment will be sterilized at 15 lbs. pressure for 20 minutes in an autoclave.
5) A sample taken prior to sterilization will be standardized using gold-leaf electroscope and G.M. tube, with reference to primary standards of uranium oxide.
6) The diluted, neutralized, sterilized, standardized solution will be administered with a calibrated sterile glass syringe, in permitted dosage.

Br^{82}. This isotope will be received as NH_4Br, and will be prepared as follows:

1) The shipment, 1.0 gm of NH_4Br, will be dissolved in 50 ml of 0.1 N $NaHCO_3$ solution, with agitation .
2) This solution will be filtered, and standardized using a gas-flow proportional counter, against uranium oxide primary standards.
3) Using this figure as a guide, the above solution will be diluted with isotonic sodium chloride solution so that each 10 ml will contain 10 microcuries of Br^{82}. This will provide a chemical dose of 2 mg of NH_4Br equivalent.
4) Phenal red will be added as indicator.
5) The material will be sterilized by autoclaving at 15 lbs. for 20 minutes.
6) 10 ml aliquots of the diluted material will be given intravenously using sterile calibrated glass syringes.

Form AEC-313 (2/57) Page Two

TRAINING AND EXPERIENCE OF EACH INDIVIDUAL NAMED IN ITEM 4 *(Use supplemental sheets if necessary)*

8. TYPE OF TRAINING	WHERE TRAINED	DURATION OF TRAINING	ON THE JOB (Circle answer)	FORMAL COURSE (Circle answer)
a. Principles and practices of radiation protection	Peter Bent Brigham Hospital Boston, Massachusetts	2 yrs	(Yes) No	Yes (No)
b. Radioactivity measurement standardization and monitoring techniques and instruments	Same	2 yrs	(Yes) No	Yes (No)
c. Mathematics and calculations basic to the use and measurement of radioactivity	Same	2 yrs	(Yes) No	Yes (No)
d. Biological effects of radiation	Same. Also U.S. Naval Radiological Defense Lab., S.F. Calif.	2yrs-9 mo	(Yes) No	Yes (No)

9. EXPERIENCE WITH RADIATION. *(Actual use of radioisotopes or equivalent experience.)*

ISOTOPE	MAXIMUM AMOUNT	WHERE EXPERIENCE WAS GAINED	DURATION OF EXPERIENCE	TYPE OF USE
K-42	3 mc	Peter Bent Brigham Hospital	2yrs	Measuring body composition in adult human beings by isotope dilution. In vitro.
Na-24	3 mc	"	2 yrs	
Br-82	9 mc	"	1 yr	
H^3	5 mc	NRDL	9 months	

10. RADIATION DETECTION INSTRUMENTS. *(Use supplemental sheets if necessary.)*

TYPE OF INSTRUMENTS (Include make and model number of each)	NUMBER AVAILABLE	RADIATION DETECTED	SENSITIVITY RANGE (mr/hr)	WINDOW THICKNESS (mg/cm^2)	USE (Monitoring, surveying, measuring)
1) Plastic well scintillation counter	1	Beta	See attached sheet 313A		Measuring
2) NaI:Tl well scintillation counter	1	Gamma	"		Measuring
3) Packard Tri-Carb Spectrometer	1	Beta	"		Measuring

11. METHOD, FREQUENCY, AND STANDARDS USED IN CALIBRATING INSTRUMENTS LISTED ABOVE.

Standard solutions of long-life isotopes

12. FILM BADGES, DOSIMETERS, AND BIO-ASSAY PROCEDURES USED. *(For film badges, specify method of calibrating and processing, or name of supplier.)*

Film badges calibrated against radium and/or cobalt 60, changed monthly. 0-200 mr pocket dosimeters used during handling of large quantities. Facilities for radioanalysis of urine available.

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. *(Circle answer)* Yes No

14. RADIATION PROTECTION PROGRAM. Describe the radiation protection program including control measures. If application covers sealed sources, submit leak testing procedures where applicable, name, training, and experience of person to perform leak tests, and arrangements for performing initial radiation survey, servicing, maintenance and repair of the source.

15. WASTE DISPOSAL. If a commercial waste disposal service is employed, specify name of company. Otherwise, submit detailed description of methods which will be used for disposing of radioactive wastes and estimates of the type and amount of activity involved.

CERTIFICATE (This item must be completed by applicant)

16. THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATE ON BEHALF OF THE APPLICANT NAMED IN ITEM 1, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PART 30, AND THAT ALL INFORMATION CONTAINED HEREIN, INCLUDING ANY SUPPLEMENTS ATTACHED HERETO, IS TRUE AND CORRECT TO THE BEST OF OUR KNOWLEDGE AND BELIEF.

Date 2/13/58

Applicant named in item 1 (b) (6)

By: (b) (6)

Acting Chairman, Radioisotope Committee

Title of certifying official

WARNING.—18 U. S. C., Section 1001; Act of June 25, 1948; 62 Stat. 749; makes it a criminal offense to make a willfully false statement or representation to any department or agency of the United States as to any matter within its jurisdiction.

U. S. GOVERNMENT PRINTING OFFICE : 1957 O-F—424006

Form AEC 313a (3/56)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE—PAGE 3

Form approved. Budget Bureau No. 38-R027.3.

This page may be completed by the physician's preceptor (if any) in the medical use of radioisotopes. When the information is not furnished by the preceptor, the name and present address of the preceptor (if any) should be shown in Item 12 below.

9. (a) Using physician's name

(b) (6) MD
LT (MC) USNR
U.S. Naval Radiological Defense Lab.
San Francisco 24, California

(b) Name & address of applicant (if different from 9 (a))

(b) (6)
Chairman, Radioisotope Committee
(Address - same)

10. Clinical Training and Experience of Physician Who Will Use Byproduct Material

A ISOTOPE	B CONDITION(S) DIAGNOSED OR TREATED	C NUMBER OF CASES	D TYPE OF PARTICIPATION FOR ALL CASES IN COLUMN C (circle applicable numbers of items in accordance with key set forth below)
I 131	Diagnosis of thyroid function		1 2 3 4
	Treatment of hyperthyroidism		1 2 3 4
	Treatment of thyroid cancer		1 2 3 4
	Treatment of cardiac conditions		1 2 3 4
	Brain tumor localization		1 2 3 4
	Blood determinations		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
P 32 Soluble	Treatment of polycythemia and leukemia		1 2 3 4
	Brain tumor localization		1 2 3 4
	Treatment of bone metastases		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
P 32 $CrPO_4$	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Au 198 Colloid	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Cr 51	Blood determinations		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Other Isotopes	Brain & Body Composition Na	150	1 2 3 4
			1 2 3 4
			1 2 3 4

Key to above numbers (Column D)

Active Participation and Discussion

1. Examination of patients to determine suitability for radioisotope diagnosis and/or treatment and recommendations on dosage to be prescribed.
2. Collaboration in calibration and administration of dosages including related measurements and plotting of data.
3. Active period of training and experience of sufficient duration to permit follow-up of patients through treatment and post-treatment period including re-evaluation as to effectiveness and complications.
4. Study and discussion of case histories to establish most efficacious diagnostic and/or therapeutic techniques for this radioisotope use.

11. Total number of hours of participation in clinical training 1 Year as Research Fellow hours

12. The training and experience indicated above was obtained under the supervision or guidance of

(b) (6) (Name of physician (preceptor)) at HARVARD (Institution)

(b) (6) (Signature)

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SUPPLEMENT 1

Item 5(b). Investigative Proposal

A. Background

Moore and co-workers (1,2,3), using isotope dilution methods, have shown that human beings can have gross altered body composition as a result of chronic disease, and that this state can be reversible following correction of the pathologic condition which caused the changes in composition. Moore has emphasized that isotope dilution methods can be used to follow long-term changes in nutrition in human beings in disease and during convalescence.

Data are available giving the results of determinations of total exchangeable sodium, total exchangeable potassium, and total exchangeable chloride in healthy adult human beings. Such values for total body water are also abundantly available. However, there is little information about the correlation of these parameters one with the other.

Recent work indicates that those aspects of body composition which are primarily aqueous, such as total exchangeable sodium, total exchangeable potassium and total exchangeable chloride, should be compared with simultaneously determined values for lean body mass (4-7) or total body water (8-9), in addition to body weight.

Edelman et al (10), studying total exchangeable potassium in edematous human beings, found that an equilibration period of 40 hours resulted in more satisfactory equilibrium than did one of 24 hours in these subjects.

In the light of these facts, there seems a need for additional measurements of total exchangeable chloride, and total exchangeable potassium, done in healthy adult human beings in conjunction with simultaneous measurements of total body water. Equilibrium periods for measurement of exchangeable potassium should be extended to 40 hours.

B. Instrumentation and Radioactivity Dose

In performing measurements of total exchangeable potassium in human beings, it has been customary to use a radioactivity dose of 250-350 microcuries of K^{42} (11, 12, 13, 14). We have constructed a counter which enables us to reduce this dose to 50 microcuries, and still measure the activity remaining at 40 hours after administration.

This counter is a plastic well scintillation counter, based on the work of Hine et al (15) and Michel et al (16), but improved so that it accepts a 10 ml volume without loss of efficiency. In liquid samples of this volume, it has an efficiency of 20% for K^{42}. By using spot urines as equilibration samples, and boiling them to 1/4th of their initial volume, we will be able to make satisfactory measurements by using 50 microcuries of K^{42}. Pilot studies justifying this dose reduction have been made with the help of Dr. Isidore S. Edelman, of University of California Medical School, San Francisco.

C. Proposed Experiments

1. Subjects. Twenty healthy adult human males and twenty healthy human females will be used as subjects. The following parameters will be determined at the same time in each subject:

Total exchangeable potassium (K^{42})
Total exchangeable chloride (Br^{82})
Total body water (H^3)

It is important to do these measurements in persons of each sex, in order to outline sex differences.

2. Isotope Doses:

K^{42}	- 50 microcuries	(0.050 rad)
Br^{82}	- 10 microcuries	(0.033 rad)
H^3	- 1 millicurie	(0.100 rad)
TOTAL		(0.183 rad)

Simultaneous administration of the above quantities of isotope will result in a dose of radioactivity within a recommended limit of 0.3 rem/week.

3. Condition for Measurement. Each subject will be in good health, and will be fasting for 12 hours prior to the time of sample collection. The women will not be measured within one week of a menstrual period, as fluid retention is associated with menstruation.

4. Administration of Dose. 20 ml of sterile, isotonic sodium chloride solution, containing the above amounts of radioactivity, will be given by vein under aseptic conditions. The individual isotope solutions will be tested biologically prior to administration.

5. The nude weight of each subject will be taken.

6. Samples:

a. Serum samples will be taken at 2 and 3 hours after administration of the dose for measurement of total body water.

b. All urine from the time of injection up to 40 hours after injection will be collected for measurement of excretion of radioactivity. Analysis will be done for K^{42} and Br^{82} activity.

c. Spot urine will be collected at 40 and 42 hours after administration for measurement of K^{42} specific activity. This will be done by differential gamma and beta counting as outlined by Hime et al (15).

d. Serum will be collected at 40 hours after administration for Br^{82} assay. Correction of the gamma count used for assay will be done by utilizing the potassium specific activity gained from the urine samples.

7. Calculations. The regression of total exchangeable potassium and total exchangeable chloride on body weight and total body water will be compared.

REFERENCES:

1. Moore, F.D.,and Ball, M.R.: Metabolic Response to Surgery, Springfield, Charles C. Thomas, 1952.

2. Moore, F.D., Edelman, I.S., Olney, J.M., James, A.A., Brooks, L., and Wilson, G.M.: Body Sodium and Potassium. III. Interrelated Trends in Alimentary, Renal, and Cardiovascular Disease, Lack of Correlation Between Body Stores and Plasma Concentration. Metabolism 3: 334, 1954.

3. Wilson, G.M., I.S. Edelman, L. Brooks, Myrden, J.A., Harken, D.E., and Moore, F.D.: Metabolic Changes Associated With Mitral Valvuloplasty. Circulation 9: 199, 1954.

4. Weir, E.G.: Further Observations on Total Chloride Content. The Relation Between Body Fat and Body Chloride. Am. J. Physiol., 130: 608, 1940.

5. Cheek, D.B., and West, D.D.: An Appraisal of Methods of Tissue Chloride Analysis: The Total Carcass Chloride, Exchangeable Chloride, Potassium and Water of the Rat. J. Clin. Invest. XXXVI, 1744, 1956.

6. Ljunggren, Hakan; Studies on Body Composition With Specific Reference to the Composition of Obesity Tissue and Non-obesity Tissue. Acta Endocrinologica, supplementum 33, 1957.

7. Muldowney, F.P., Crooks, J., and Bluhm, M.M. The Relationship of Total Exchangeable Potassium and Chloride to Lean Body Mass, Red Cell Mass and Creatinine Excretion in Man. J. Clin. Invest. XXXVI, 1375, 1957.

8. Anderson, E.C., Schuck, R.L., Perrings, J.D., and Langham, W.H. The Los Alamos Human Counter. Nucleonics, 1956, 14, 14 (No. 1).

9. Boling, E.A., Wilson, G.M., Dudley, H.A.F., and Moore, F.D. The Bromide Space and Total Exchangeable Chloride: Their Determination With Br^{82} and Their Relationship to the Total Body Water. To be published.

10. O'Meara, M.P., Birkenfeld, L.W., Gotch, F.A., and Edelman, I.S. The Equilibration of Radiosodium (Na^{24}), Radiopotassium (K^{42}), and Deuterium Oxide (D_2O) in Hydropic Human Subjects. J. Clin. Invest. 1957, 36, 784.

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11. Arons, W.L., Vanderline, R.J., and Solomon, A.K. II. The Simultaneous Measurement of Exchangeable Body Sodium and Potassium Utilizing Ion Exchange Chromatography. J. Clin. Invest. XXXIII, 1001, 1954.

12. Robinson, C.V., Arons, W.L., and Solomon, A.K. An Improved Method for Simultaneous Determination of Exchangeable Body Sodium and Potassium. J. Clin. Invest. XXXIV, 134, 1955.

13. James, A.H. Brooks, L., Edelman, I.S., Olney, J.M., and Moore, F.D. Body Sodium and Potassium. I. Simultaneous Measurement of Exchangeable Sodium and Potassium in Man by Isotope Dilution. Metabolism, 1954, 3, 313.

14. Corsa, L., Jr., Olney, J.M., Jr., Steenburg, R.W., Ball, M.R., and Moore, F.D. The Measurement of Exchangeable Potassium in Man by Isotope Dilution. J. Clin. Invest. 1950, 29, 1280.

15. Hine, G.J., Burrows, B.A., Apt, L., Pollycove, M., Ross, J.F., and Sarkes, L.A. Scintillation Counting for Multiple-tracer Studies. Nucleonics, 13: 23, 1955.

16. Michel, W.D., Brownell, G.L., and Mealey, J., Jr. Designing Sensitive Plastic-well Counters for Beta Rays. Nucleonics, 14: 96, 1956.